=> d ibib abs hitstr 18 1

ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2005:316356 HCAPLUS Full-text

DOCUMENT NUMBER: 142:367666

TITLE: Compositions and methods using farnesoid X receptor

agonists for treatment of fibrosis

INVENTOR(S): Liu, Yaping; Moore, John Tomlin

PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA; Jones, Stacey Ann

SOURCE: PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

	PATENT NO.				KIND DATE				APPLICATION NO.						DATE				
,	wo	2005	0325	 49		A1	_	2005			WO 2	004-	US29	748					
		W:	ΑE,	AG,	AL,	AM,	ΑT,	ΑU,	AZ,	BA,	BB,	ВG,	BR,	BW,	BY,	BZ,	CA,	CH,	
			CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,	
			GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	KΖ,	LC,	
			LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,	ΝI,	
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		RW:	BW,	GH,	GM,	ΚE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	
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			SI,	SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	ΝE,	
			SN,	TD,	ΤG														
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PRIOR	PRIORITY APPLN. INFO.:				.:						US 2	003-	5063	94P		P 2	0030	926	
											WO 2	004-	US29	748	,	W 2	0040	910	
OTHED	0.0	TIDOE.	(C).			MAD.	יייער	140.	2070										

MARPAT 142:367666

Methods for the treatment of fibrosis, including liver fibrosis, via administration of FXR agonists are provided. FXR agonist GW4064 reduced collagen deposition in livers of rats treated with CCl4.

517-28-2 635-65-4 9000-86-6 9000-97-9 9001-60-9 9001-78-9 9002-02-2 9003-98-9 9046-27-9 65666-07-1 192526-67-3 17372-87-1

RL: PRPH (Prophetic)

(Compositions and methods using farnesoid X receptor agonists for treatment of fibrosis)

RN 517-28-2 HCAPLUS

CN Benz[b]indeno[1,2-d]pyran-3,4,6a,9,10(6H)-pentol, 7,11b-dihydro-, (6aS, 11bR) - (CA INDEX NAME)

Absolute stereochemistry.

RN 635-65-4 HCAPLUS

CN 21H-Biline-8,12-dipropanoic acid, 2,17-diethenyl-1,10,19,22,23,24-hexahydro-3,7,13,18-tetramethyl-1,19-dioxo- (CA INDEX NAME)

Double bond geometry as shown.

RN 9000-86-6 HCAPLUS

CN Aminotransferase, alanine (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 9000-97-9 HCAPLUS

CN Aminotransferase, aspartate (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 9001-60-9 HCAPLUS

CN Dehydrogenase, lactate (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 9001-78-9 HCAPLUS

CN Phosphatase, alkaline (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 9002-02-2 HCAPLUS

CN Dehydrogenase, succinate (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 9003-98-9 HCAPLUS

CN Nuclease, deoxyribo- (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 9046-27-9 HCAPLUS

CN Glutamyltransferase, γ- (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 17372-87-1 HCAPLUS

CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthen]-3-one,

2',4',5',7'-tetrabromo-3',6'-dihydroxy-, sodium salt (1:2) (CA INDEX NAME)

●2 Na

RN 65666-07-1 HCAPLUS

CN Silymarin (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 192526-67-3 HCAPLUS

CN TRIzol (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

IT 278779-30-9, GW4064

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);

THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(as farnesoid X receptor agonist; farnesoid X receptor agonists for treatment of fibrosis)

RN 278779-30-9 HCAPLUS

CN Benzoic acid, 3-[2-[2-chloro-4-[[3-(2,6-dichlorophenyl)-5-(1-methylethyl)-4-isoxazolyl]methoxy]phenyl]ethenyl]- (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

HO2C

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140208-24-8, TIMP1
    RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (farnesoid X receptor agonists for treatment of #ibrosis)
RN
    140208-24-8 HCAPLUS
CN
    Proteinase inhibitor, TIMP 1 (CA INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
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    849654-20-2 849654-21-3 849654-22-4
    849654-23-5 849654-24-6
                             849654-25-7
    849654-26-8 849654-27-9
                              849654-28-0
                 849654-30-4 849654-31-5
    849654-29-1
    RL: PRP (Properties)
       (unclaimed nucleotide sequence; compns. and methods using farnesoid X
       receptor agonists for treatment of fibrosis)
RN
    849654-17-7 HCAPLUS
    DNA, d(T-C-C-T-G-A-C-C-T-G-A-A-G-T-A-T-C-C-G-A-T-A) (9CI) (CA INDEX
CN
    NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
    849654-18-8 HCAPLUS
CN
    DNA, d(G-G-T-G-C-C-A-G-A-T-C-T-T-T-T-C-C-A-T-G-T-C) (9CI) (CA INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
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CN
    DNA, d(A-A-C-A-C-G-G-C-A-T-C-A-T-C-A-C-C-A-A-C-T-G-G-G-A) (9CI) (CA INDEX
    NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
    849654-20-2 HCAPLUS
RN
    DNA, d(T-T-C-A-C-C-T-A-C-A-G-C-A-C-G-C-T-T-G-T-G) (9CI) (CA INDEX NAME)
CN
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
    849654-21-3 HCAPLUS
RN
CN
    DNA, d(G-A-T-G-A-C-T-G-T-C-T-T-G-C-C-C-A-A-G-T-T) (9CI) (CA INDEX NAME)
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RN
    DNA, d(A-T-G-G-C-T-G-C-A-C-G-A-G-T-C-A-C-A-C-G) (9CI) (CA INDEX NAME)
CN
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    849654-23-5 HCAPLUS
    DNA, d(C-C-A-A-A-G-C-C-A-C-C-G-G-A-G-T-C-T-T) (9CI) (CA INDEX NAME)
CN
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
    849654-24-6 HCAPLUS
RN
    DNA, d(G-C-T-T-G-A-A-G-C-C-A-A-T-C-C-T-T-G-G-A) (9CI) (CA INDEX NAME)
CN
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
    849654-25-7 HCAPLUS
RN
CN
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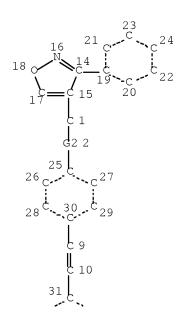
\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

(CA INDEX NAME)

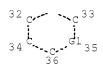
- RN 849654-26-8 HCAPLUS
- CN DNA, d(G-A-A-C-C-G-C-A-G-C-G-A-G-G-A-G-T-T-T) (9CI) (CA INDEX NAME)
- \*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*
- RN 849654-27-9 HCAPLUS
- CN DNA, d(G-G-C-A-G-T-G-A-T-G-T-G-C-A-A-A-T-T-T-C-C) (9CI) (CA INDEX NAME)
- \*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*
- RN 849654-28-0 HCAPLUS
- CN DNA, d(T-C-A-T-C-G-C-G-G-C-C-G-T-T-T-A-A-G-G-A-A) (9CI) (CA INDEX NAME)
- \*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*
- RN 849654-29-1 HCAPLUS
- CN DNA, d(G-C-T-G-C-T-G-A-C-C-C-C-C-A-C-T-G-A-T) (9CI) (CA INDEX NAME)
- \*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*
- RN 849654-30-4 HCAPLUS
- CN DNA, d(G-C-C-A-C-T-G-C-C-G-G-A-C-A-A-C-T-C) (9CI) (CA INDEX NAME)
- \*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*
- RN 849654-31-5 HCAPLUS
- CN DNA, d(C-G-C-T-G-A-G-T-G-G-C-T-G-T-C-T-T-T-T-G-A-C-G-T) (9CI) (CA INDEX NAME)
- \*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*
- REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

## RESULTS FROM REGISTRY AND CAPLUS

=> d que stat 114 L9 STR



Page 1-A



Page 2-A
VAR G1=CH/N
VAR G2=O/NH
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED NUMBER OF NODES IS 27

STEREO ATTRIBUTES: NONE

L11 45 SEA FILE=REGISTRY SSS FUL L9

L14 10 SEA FILE=HCAPLUS ABB=ON L11 AND (?LIVER? OR ?HEPAT?)(W)(?DISEA S? OR ?FIBROSIS?)

=> d ibib abs hitstr 114 1-10

L14 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2006:383580 HCAPLUS <u>Full-text</u>

DOCUMENT NUMBER: 144:404429

TITLE: A method using farnesoid X receptor (FXR) agonists

with PPAR agonists for reducing drug-induced adverse

side effects in a patient

INVENTOR(S): Fiorucci, Stefano; Pellicciari, Roberto; Pruzanski,

Mark

PATENT ASSIGNEE(S): Intercept Pharmaceuticals Inc., USA

SOURCE: PCT Int. Appl., 35 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PAT	PATENT NO.					KIND DATE				APPLICATION NO.									
WO	2006	0443	91		A1		2006	0427							2	0051	014		
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		NA,	NG,	NΙ,	NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,		
		SK,	SL,	SM,	SY,	ТJ,	TM,	TN,	TR,	TΤ,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,		
		YU,	ZA,	ZM,	ZW														
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		CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	$ ext{ML}$ ,	MR,	ΝE,	SN,	TD,	TG,	BW,	GH,		
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		•	•	•	RU,	•													
	2006																		
AU	2005															0051			
	2584										005-								
EP	1814															0051			
	R:		•	•				•			ES,		,		•	,	•		
											PT,								
	2008				Τ		2008	0522											
RIORIT	APP:	LN.	INFO	.:							004-								
									,	WO 2	005-1	US36.	536	Ī	W 2	0051	014		

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention relates to the discovery that farnesoid X receptor (FXR) agonists can be used in combination with peroxisome proliferation activated receptor  $\gamma$  (PPAR $\gamma$ ) agonists to reduce drug-induced adverse side effects in patients suffering from conditions such as insulin resistance, Type II diabetes, metabolic syndrome, non-alc. fatty liver disease (NAFLD), non-alc. steatohepatitis (NASH), and heart disease. Particularly, the invention encompasses methods for treating patients suffering from drug-induced adverse side effects with selective PPAR $\gamma$ , dual PPARa/ $\gamma$  and pan PPAR $\alpha/\gamma/\delta$  agonists in combination with FXR agonists.

IT 278779-30-9, GW4064

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(FXR agonist combination with PPAR agonist for reduction of drug-induced adverse effects)

RN 278779-30-9 HCAPLUS

CN Benzoic acid, 3-[2-[2-chloro-4-[[3-(2,6-dichlorophenyl)-5-(1-methylethyl)-4-isoxazolyl]methoxy]phenyl]ethenyl]- (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

H02C

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD

(1 CITINGS)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2005:1077095 HCAPLUS Full-text

DOCUMENT NUMBER: 143:339369

TITLE: Cross-talk between farnesoid-X-receptor (FXR) and

peroxisome proliferator-activated receptor  $\gamma$  contributes to the antifibrotic activity of FXR ligands in rodent models of liver cirrhosis

AUTHOR(S): Fiorucci, Stefano; Rizzo, Giovanni; Antonelli, Elisabetta; Renga, Barbara; Mencarelli, Andrea;

Riccardi, Luisa; Morelli, Antonio; Pruzanski, Mark;

Pellicciari, Roberto

CORPORATE SOURCE: Dipartimento di Medicina Clinica e Sperimentale,

Universita degli Studi di Perugia, Perugia, Italy

SOURCE: Journal of Pharmacology and Experimental Therapeutics

(2005), 315(1), 58-68

CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental

Therapeutics

DOCUMENT TYPE: Journal LANGUAGE: English

AB The nuclear receptors farnesoid X receptor (FXR) and peroxisome proliferatoractivated receptor (PPAR)γ exert counterregulatory effects on hepatic stellate
cells (HSCs) and protect against liver fibrosis development in rodents. Here,
we investigated whether FXR ligands regulate PPARγ expression in HSCs and
models of liver fibrosis induced in rats by porcine serum and carbon

tetrachloride administration and bile duct ligation. Our results demonstrate that HSCs trans-differentiation associated with suppression of PPARy mRNA expression, whereas FXR mRNA was unchanged. Exposure of cells to natural and synthetic ligands of FXR, including 6-Et chenodeoxycholic acid (6-ECDCA), a synthetic derivative of chenodeoxycholic acid, reversed this effect and increased PPAR $\gamma$  mRNA by pprox 40-fold. Submaximally effective concns. of FXR and PPARy ligands were additive in inhibiting  $\alpha 1(I)$  collagen mRNA accumulation induced by transforming growth factor (TGF) $\beta$ 1. Administration of 6-ECDCA in rats rendered cirrhotic by porcine serum and carbon tetrachloride administration or bile duct ligation reverted down-regulation of PPARy mRNA expression in HSCs. Cotreatment with 6-ECDCA potentiates the antifibrotic activity of rosiglitazone, a PPARy ligand, in the porcine serum model as measured by morphometric anal. of liver collagen content, hydroxyproline, and liver expression of  $\alpha 1(I)$  collagen mRNA,  $\alpha$ -smooth muscle actin, fibronectin,  $\mathsf{TGF}\beta 1$ , and tissue inhibitor of metalloprotease 1 and 2, whereas it enhanced the expression of PPARy and uncoupling protein 2, a PPARy-regulated gene, by 2fold. In conclusion, by using an in vitro and in vivo and in vivo approach, we demonstrated that FXR ligands up-regulate PPARy mRNA in HSCs and in rodent models of liver fibrosis. A FXR-PPARy cascade exerts counter-regulatory effects in HSCs activation.

IT 278779-30-9, GW 4064

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antifibrotic activity of FXR ligands mediated by cross-talk between FXR and PPARy in rodent liver cirrhosis model)

278779-30-9 HCAPLUS

RN

CN

Benzoic acid, 3-[2-[2-chloro-4-[[3-(2,6-dichlorophenyl)-5-(1-methylethyl)-4-isoxazolyl]methoxy]phenyl]ethenyl]- (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

OS.CITING REF COUNT: 32 THERE ARE 32 CAPLUS RECORDS THAT CITE THIS

RECORD (32 CITINGS)

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

APPLICATION NO.

DATE

L14 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:1049799 HCAPLUS Full-text

DOCUMENT NUMBER: 143:319188

TITLE: Treatment of fibrosis using farnesoid X receptor (FXR)

ligands

INVENTOR(S): Fiorucci, Stefano; Pellicciari, Roberto; Pruzanski,

Mark

KIND

PATENT ASSIGNEE(S): Intercept Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 70 pp.

CODEN: PIXXD2

DATE

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.

111.																		
WO	2005089316		A2	20050929		WO 2005-US8575					20050314							
WO	2005	0893	16		А3		2006	0406										
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		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	KΖ,	LC,	
		LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,	NΙ,	
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		EE,	ES,	FI,	FR,	GB,	GR,	HU,	IE,	IS,	ΙΤ,	LT,	LU,	MC,	NL,	PL,	PT,	
		RO,	SE,	SI,	SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	G₩,	${ m ML}$ ,	
		MR,	NE,	SN,	TD,	ΤG												
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CA	2559	476			A1		2005	0929	(	CA 2	005-	2559	476		2	0050	314	
			070		A1		2006	0330	US 2005-81002					20050314				
EP	1734	970			A2		2006	1227		EP 2	005-	7293	94		2	0050	314	
	R:		•				CZ,								•	HU,	IE,	
		IS,	ΙT,	LI,	LT,	LU,	MC,	NL,	PL,	PT,	RO,	SE,	SI,	SK,	TR			
JP	2007	5294	27		Τ		2007	1025				5031				0050		
RIORIT	ORITY APPLN. INFO.:								US 2004-552865P P 20040312									
WO 2005-US8575 W 20050314																		

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention discloses a method for inhibiting fibrosis that occurs in an organ where the farnesoid X receptor (FXR) is expressed. The method involves administering a high potency, activating ligand of FXR in an effective amount to a patient who is not suffering from a cholestatic condition. The invention also provides pharmaceutical compns. containing an effective amount of an FXR ligand and kits for dispensing the pharmaceutical compns.

IT 278779-30-9, GW4064

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(farnesoid X receptor ligands for treatment of fibrosis)

RN 278779-30-9 HCAPLUS

CN Benzoic acid, 3-[2-[2-chloro-4-[[3-(2,6-dichlorophenyl)-5-(1-methylethyl)-4-isoxazolyl]methoxy]phenyl]ethenyl]- (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

HO2C

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2005:413517 HCAPLUS Full-text

DOCUMENT NUMBER: 142:441633

TITLE: Protective effects of 6-ethyl chenodeoxycholic acid, a

farnesoid X receptor ligand, in estrogen-induced

cholestasis

AUTHOR(S): Fiorucci, Stefano; Clerici, Carlo; Antonelli,

Elisabetta; Orlandi, Stefano; Goodwin, Bryan; Sadeghpour, Bahman M.; Sabatino, Giuseppe; Russo, Giuseppe; Castellani, Danilo; Willson, Timothy M.; Pruzanski, Mark; Pellicciari, Roberto; Morelli,

Antonio

CORPORATE SOURCE: Clinica di Gastroenterologia ed Epatologia,

Dipartimento di Medicina Clinica e Sperimentale
Universita degli Studi di Perugia, Perugia, Italy

SOURCE: Journal of Pharmacology and Experimental Therapeutics

(2005), 313(2), 604-612

CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental

Therapeutics

DOCUMENT TYPE: Journal LANGUAGE: English

The farnesoid X receptor (FXR), an endogenous sensor for bile acids, regulates a program of genes involved in bile acid biosynthesis, conjugation, and transport. Cholestatic liver diseases are a group of immunol. and genetically mediated disorders in which accumulation of endogenous bile acids plays a role in the disease progression and symptoms. Here, the authors describe the

effect of 6-Et chenodeoxycholic acid (6-ECDCA or INT-747), a semisynthetic bile acid derivative and potent FXR ligand, in a model of cholestasis induced by 5-day administration of  $17\alpha$ -ethynylestradiol (E2  $17\alpha$ ) to rats. exposure of rat hepatocytes to 1  $\mu$ M 6-ECDCA caused a 3- to 5-fold induction of small heterodimer partner (Shp) and bile salt export pump (bsep) mRNA and 70 to 80% reduction of cholesterol  $7\alpha$ -hydroxylase (cyp7a1), oxysterol  $12\beta$ hydroxylase (cyp8b1), and Na+/taurocholate cotransporting peptide (ntcp). In vivo administration of 6-ECDCA protects against cholestasis induced by E2  $17\alpha$ . Thus, 6-ECDCA reverted bile flow impairment induced by E2  $17\alpha$ , reduced secretion of cholic acid and deoxycholic acid, but increased muricholic acid and chenodeoxycholic acid secretion. In vivo administration of 6-ECDCA increased liver expression of Shp, bsep, multidrug resistance-associated protein-2, and multidrug resistance protein-2, whereas it reduced cyp7a1 and cyp8b1 and ntcp mRNA. These changes were reproduced by GW4064, a synthetic FXR ligand. In conclusion, by demonstrating that 6-ECDCA protects against E2  $17\alpha$  cholestasis, the authors' data support the notion that development of potent FXR ligands might represent a new approach for the treatment of cholestatic disorders.

IT 278779-30-9, GW4064

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); BIOL (Biological study)

(chenodeoxycholic acid derivative protection against estrogen-induced cholestasis and mechanisms thereof)

RN 278779-30-9 HCAPLUS

CN

Benzoic acid, 3-[2-[2-chloro-4-[[3-(2,6-dichlorophenyl)-5-(1-methylethyl)-4-isoxazolyl]methoxy]phenyl]ethenyl]- (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

HO2C/

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2005:316356 HCAPLUS  $\underline{\text{Full-text}}$ 

DOCUMENT NUMBER: 142:367666

TITLE: Compositions and methods using farnesoid X receptor

agonists for treatment of fibrosis  $% \left( \frac{1}{2}\right) =\frac{1}{2}\left( \frac{1}{2}\right)$ 

INVENTOR(S): Liu, Yaping; Moore, John Tomlin

PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA; Jones, Stacey Ann

SOURCE: PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

P	PATENT NO.			KIND DATE				APPLICATION NO.						DATE				
M	2005				A1	_			1									
	W:	ΑE,	AG,	AL,	AM,	ΑT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH,	
		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FΙ,	GB,	GD,	
		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	KΖ,	LC,	
		LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,	NI,	
		NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,	
		ТJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW	
	RW:	BW,	GH,	GM,	ΚE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	
		ΑZ,	BY,	KG,	KΖ,	MD,	RU,	ТJ,	TM,	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	
		EE,	ES,	FI,	FR,	GB,	GR,	HU,	ΙE,	ΙΤ,	LU,	MC,	NL,	PL,	PT,	RO,	SE,	
		SI,	SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	ΝE,	
		SN,	TD,	TG														
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	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	ΙΤ,	LI,	LU,	NL,	SE,	MC,	PT,	
		ΙE,	SI,	LT,	LV,	FΙ,	RO,	CY,	TR,	BG,	CZ,	EE,	HU,	PL,	SK,	HR		
U	US 20070015796				A1	A1 20070118				US 2	006-	5729	20060322					
PRIORI'	RIORITY APPLN. INFO.:								1	US 2003-506394P					P 20030926			
									1	WO 2	004-1	JS29	748	Ţ	w 2	0040	910	

OTHER SOURCE(S): MARPAT 142:367666

AB Methods for the treatment of fibrosis, including liver fibrosis, via administration of FXR agonists are provided. FXR agonist GW4064 reduced collagen deposition in livers of rats treated with CCl4.

IT 278779-30-9, GW4064

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(as farnesoid X receptor agonist; farnesoid X receptor agonists for treatment of fibrosis)

RN 278779-30-9 HCAPLUS

CN Benzoic acid, 3-[2-[2-chloro-4-[[3-(2,6-dichlorophenyl)-5-(1-methylethyl)-4-isoxazolyl]methoxy]phenyl]ethenyl]- (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

H02C

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2004:1061036 HCAPLUS Full-text

DOCUMENT NUMBER: 142:232933

TITLE: The nuclear receptor SHP mediates inhibition of hepatic stellate cells by FXR and protects against

liver fibrosis

AUTHOR(S): Fiorucci, Stefano; Antonelli, Elisabetta; Rizzo,

Giovanni; Renga, Barbara; Mencarelli, Andrea; Riccardi, Luisa; Orlandi, Stefano; Pellicciari,

Roberto; Morelli, Antonio

CORPORATE SOURCE: Dipartimento di Medicina Clinica e Sperimentale,

Clinica di Gastroenterologia ed Endoscopia Digestiva,

Perugia, Italy

SOURCE: Gastroenterology (2004), 127(5), 1497-1512

CODEN: GASTAB; ISSN: 0016-5085

PUBLISHER: Elsevier Inc.

DOCUMENT TYPE: Journal LANGUAGE: English

Background & Aims: The farnesoid X receptor (FXR) is an endogenous sensor for bile acids and inhibits bile acid synthesis by inducing small heterodimer partner (SHP) gene expression. The aim of this study was to investigate whether FXR is expressed by and modulates function of hepatic stellate cells (HSCs). Methods: The antifibrotic activity of FXR ligand was tested in 2 rodent models: the porcine serum and bile duct ligation (BDL). Results: Twelve-week administration of 1-10 mg/kg 6-Et chenodeoxycholic acid (6-ECDCA), a synthetic FXR ligand, to porcine serum-treated rats prevented liver fibrosis development and reduced liver expression of  $\alpha$ 1(I) collagen, TGF- $\beta$ 1 and  $\alpha$ -SMA

mRNA by .apprx.90%. Therapeutic administration of 6-ECDCA, 3 mg/kg, to BDL rats reduced liver fibrosis and  $\alpha l(I)$  collagen, transforming growth factor (TGF)- $\beta l$ ,  $\alpha$ -SMA, and tissue metalloproteinase inhibitor (TIMP)-1 and 2 mRNA (mRNA) by 70%-80%. No protection was observed in BDL rats treated with CDCA, 3 mg/kg, and ursodeoxycholic acid, 15 mg/kg. FXR expression was detected in HSCs. Exposure of HSCs to FXR ligands caused a 3-fold increase of SHP, reduced  $\alpha l(I)$  collagen and TGF- $\beta l$  by .apprx.60%-70% and abrogates  $\alpha l(I)$  collagen mRNA up-regulation induced by thrombin and TGF- $\beta l$ . By retrovirus infection and small interference RNA, we generated SHP overexpressing and SHP-deficient HSC-T6. Using these cell lines, we demonstrated that SHP binds JunD and inhibits DNA binding of adaptor protein (AP)-1 induced by thrombin. Conclusions: By demonstrating that an FXR-SHP regulatory cascade promotes resolution of liver fibrosis, this study establish that FXR ligands might represent a novel therapeutic option to treat liver fibrosis.

IT 278779-30-9, GW4064

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(GW4064 reduced  $\alpha 1 \, \text{(l)}$  collagen in HSCs and immortalized HSP-T6 cell line)

RN 278779-30-9 HCAPLUS

CN Benzoic acid, 3-[2-[2-chloro-4-[[3-(2,6-dichlorophenyl)-5-(1-methylethyl)-4-isoxazolyl]methoxy]phenyl]ethenyl]- (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

HO2C

OS.CITING REF COUNT: 63 THERE ARE 63 CAPLUS RECORDS THAT CITE THIS

RECORD (64 CITINGS)

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:630391 HCAPLUS Full-text

DOCUMENT NUMBER: 142:273060

TITLE: The nuclear bile acid receptor FXR as a novel

therapeutic target in cholestatic liver

diseases: Hype or hope?

AUTHOR(S): Trauner, Michael

CORPORATE SOURCE: Laboratory of Experimental and Molecular Hepatology,

Division of Gastroenterology and Hepatology,

Department of Internal Medicine, Medical University

Graz, Graz, Austria

SOURCE: Hepatology (Hoboken, NJ, United States) (2004), 40(1),

260-263

CODEN: HPTLD9; ISSN: 0270-9139

PUBLISHER: John Wiley & Sons, Inc. DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. A polemic in response to Liu et al. (J. Clin. Invest., 2003, 112, 1678-1687) is presented. Liu et al. investigated the effects of the farnesoid X receptor agonist GW4064 and tauroursodeoxycholic acid (TUDCA) as clin. comparator in  $\alpha$ -naphthylisothiocyanate (ANIT)-treated and common bile duct ligated (CBDL) rats as models of intrahepatic and extrahepatic cholestasis, resp. Some of conceptual and methodol. limitations of the study of Liu et al. are discussed. However, despite these limitations, their study indicates an important new direction in the treatment of cholestasis. This concept needs to be refined by the use of more gene-selective agonists and combination approaches targeting both regular/orthograde (FXR-dependent) and alternative/retrograde pathways of bile acid transport and metabolism IT 278779-30-9, GW4064

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (nuclear bile acid receptor FXR as therapeutic target in cholestatic liver diseases)

RN 278779-30-9 HCAPLUS

CN Benzoic acid, 3-[2-[2-chloro-4-[[3-(2,6-dichlorophenyl)-5-(1-methylethyl)-4-isoxazolyl]methoxy]phenyl]ethenyl]- (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

HO2C

THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD OS.CITING REF COUNT:

(5 CITINGS)

REFERENCE COUNT: 2.3 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2003:973413 HCAPLUS Full-text

DOCUMENT NUMBER: 140:229012

TITLE: Hepatoprotection by the farnesoid X receptor agonist

GW4064 in rat models of intra- and extrahepatic

cholestasis

Liu, Yaping; Binz, Jane; Numerick, Mary Jo; Dennis, AUTHOR(S):

Steve; Luo, Guizhen; Desai, Bhasha; MacKenzie,

Kathleen I.; Mansfield, Traci A.; Kliewer, Steven A.;

Goodwin, Bryan; Jones, Stacey A.

CORPORATE SOURCE: Nuclear Receptor Functional Analysis, High Throughput

Biology, GlaxoSmithKline, Research Triangle Park, NC,

USA

SOURCE: Journal of Clinical Investigation (2003), 112(11),

1678-1687

CODEN: JCINAO; ISSN: 0021-9738

PUBLISHER: American Society for Clinical Investigation

DOCUMENT TYPE: Journal LANGUAGE: English

AΒ Farnesoid X receptor (FXR) is a bile acid-activated transcription factor that is a member of the nuclear hormone receptor superfamily. Fxr-null mice exhibit a phenotype similar to Byler disease, an inherited cholestatic liver disorder. In the liver, activation of FXR induces transcription of transporter genes involved in promoting bile acid clearance and represses genes involved in bile acid biosynthesis. We investigated whether the synthetic FXR agonist GW4064 could protect against cholestatic liver damage in rat models of extrahepatic and intrahepatic cholestasis. In the bile ductligation and  $\alpha$ -naphthylisothiocyanate models of cholestasis, GW4064 treatment resulted in significant redns. in serum alanine aminotransferase, aspartate aminotransferase, and lactate dehydrogenase, as well as other markers of liver damage. Rats that received GW4064 treatment also had decreased incidence and extent of necrosis, decreased inflammatory cell infiltration, and decreased bile duct proliferation. Anal. of gene expression in livers from  ${\tt GW4064-}$ treated cholestatic rats revealed decreased expression of bile acid biosynthetic genes and increased expression of genes involved in bile acid transport, including the phospholipid flippase MDR2. The hepatoprotection seen in these animal models by the synthetic FXR agonist suggests FXR agonists may be useful in the treatment of cholestatic liver disease.

ΙT 278779-30-9, GW4064

> RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(hepatoprotection by farnesoid X receptor agonist GW4064 in rat models of intra- and extrahepatic cholestasis)

278779-30-9 HCAPLUS RN

CN Benzoic acid, 3-[2-[2-chloro-4-[[3-(2,6-dichlorophenyl)-5-(1-methylethyl)-4-isoxazolyl|methoxy|phenyl|ethenyl|- (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

HO2C

OS.CITING REF COUNT: 107 THERE ARE 107 CAPLUS RECORDS THAT CITE THIS

RECORD (107 CITINGS)

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2003:855658 HCAPLUS Full-text

DOCUMENT NUMBER: 139:317457

TITLE: Compositions and methods using farnesoid X receptor

ligands for hepatoprotection and treatment of

cholestasis

INVENTOR(S): Kliewer, Steven Anthony; Willson, Timothy Mark

PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 8 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO.	DATE
US 20030203939	A1 200310	030 US 2002-132311	20020425
US 6987121	B2 200601	.17	
WO 2003090745	A1 200313	LO6 WO 2003-US10519	20030407
W: AE, AG, AL	, AM, AT, AU, A	AZ, BA, BB, BG, BR, BY,	BZ, CA, CH, CN,
CO, CR, CU	, CZ, DE, DK, I	DM, DZ, EC, EE, ES, FI,	GB, GD, GE, GH,
GM, HR, HU	, ID, IL, IN,	IS, JP, KE, KG, KP, KR,	KZ, LC, LK, LR,
LS, LT, LU	, LV, MA, MD, N	MG, MK, MN, MW, MX, MZ,	NI, NO, NZ, OM,
PH, PL, PT	, RO, RU, SC, S	SD, SE, SG, SK, SL, TJ,	TM, TN, TR, TT,
TZ, UA, UG	, US, UZ, VC, V	N, YU, ZA, ZM, ZW	

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG AU 2003226283 20031110 AU 2003-226283 Α1 20030407 EP 1501506 Α1 20050202 EP 2003-747270 20030407 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK PRIORITY APPLN. INFO.: US 2002-132311 A 20020425 WO 2003-US10519 W 20030407

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT OTHER SOURCE(S): MARPAT 139:317457

AB Methods for the treatment of cholestatic liver disease and reduction and prevention of hepatic injury resulting from cholestasis via administration of a FXR ligand are provided. Bile duct-ligated rats treated with FXR ligand GW4064 had a pronounced improvement in liver function as defined by a reduction in a panel of liver disease serum marker enzymes.

IT 278779-30-9, GW4064

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (FXR agonist; farnesoid X receptor ligands for hepatoprotection and treatment of cholestasis)

RN 278779-30-9 HCAPLUS

CN Benzoic acid, 3-[2-[2-chloro-4-[[3-(2,6-dichlorophenyl)-5-(1-methylethyl)-4-isoxazolyl]methoxy]phenyl]ethenyl]- (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

HO2C/

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2002:677926 HCAPLUS <u>Full-text</u>

DOCUMENT NUMBER: 138:49877

TITLE: Lithocholic acid decreases expression of bile salt export pump through farnesoid X receptor antagonist

activity

AUTHOR(S): Yu, Jinghua; Lo, Jane-L.; Huang, Li; Zhao, Annie;

Metzger, Edward; Adams, Alan; Meinke, Peter T.;

Wright, Samuel D.; Cui, Jisong

CORPORATE SOURCE: Department of Atherosclerosis and Endocrinology, Merck

Research Laboratories, Rahway, NJ, 07065, USA

SOURCE: Journal of Biological Chemistry (2002), 277(35),

31441-31447

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular

Biology

DOCUMENT TYPE: Journal LANGUAGE: English

Bile salt export pump (BSEP) is a major bile acid transporter in the liver. Mutations in BSEP result in progressive intrahepatic cholestasis, a severe liver disease that impairs bile flow and causes irreversible liver damage. BSEP is a target for inhibition and down-regulation by drugs and abnormal bile salt metabolites, and such inhibition and down-regulation may result in bile acid retention and intrahepatic cholestasis. In this study, we quant. analyzed the regulation of BSEP expression by FXR ligands in primary human hepatocytes and HepG2 cells. We demonstrate that BSEP expression is dramatically regulated by ligands of the nuclear receptor farnesoid X receptor (FXR). Both the endogenous FXR agonist chenodeoxycholate (CDCA) and synthetic FXR ligand GW4064 effectively increased BSEP mRNA in both cell types. This up-regulation was readily detectable at as early as 3 h, and the ligand potency for BSEP regulation correlates with the intrinsic activity on FXR. These results suggest BSEP as a direct target of FXR and support the recent report that the BSEP promoter is transactivated by FXR. In contrast to CDCA and GW4064, lithocholate (LCA), a hydrophobic bile acid and a potent inducer of cholestasis, strongly decreased BSEP expression. Previous studies did not identify LCA as an FXR antagonist ligand in cells, but we show here that LCA is an FXR antagonist with partial agonist activity in cells. In an in vitro coactivator association assay, LCA decreased CDCA- and GW4064-induced FXR activation with an IC50 of 1  $\mu$ M. In HepG2 cells, LCA also effectively antagonized GW4064-enhanced FXR transactivation. These data suggest that the toxic and cholestat effect of LCA in animals may result from its downregulation of BSEP through FXR. Taken together, these observations indicate that FXR plays an important role in BSEP gene expression and that FXR ligands may be potential therapeutic drugs for intrahepatic cholestasis.

IT 278779-30-9, GW4064

RL: BSU (Biological study, unclassified); BIOL (Biological study) (endogenous FXR agonist chenodeoxycholate and synthetic FXR ligand GW4064 effectively increases BSEP (bile salt export pump) mRNA in primary human hepatocytes and HepG2 cells)

RN 278779-30-9 HCAPLUS

CN Benzoic acid, 3-[2-[2-chloro-4-[[3-(2,6-dichlorophenyl)-5-(1-methylethyl)-4-isoxazolyl]methoxy]phenyl]ethenyl]- (CA INDEX NAME)

10/572,974

12/3/09

PAGE 1-A

PAGE 2-A

HO2C/

OS.CITING REF COUNT: 65 THERE ARE 65 CAPLUS RECORDS THAT CITE THIS RECORD (66 CITINGS)

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

## SEARCH HISTORY

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L5

L8

L9

(FILE 'HOME' ENTERED AT 10:21:03 ON 03 DEC 2009)

FILE 'HCAPLUS' ENTERED AT 10:21:18 ON 03 DEC 2009

E JONES STACEY ANN/AU

L133 SEA ABB=ON ("JONES STACEY"/AU OR "JONES STACEY A"/AU OR "JONES STACEY ANN"/AU)

E LIU YAPING/AU

L2 131 SEA ABB=ON "LIU YAPING"/AU

E MOORE JOHN TOMLIN/AU

124 SEA ABB=ON ("MOORE JOHN T"/AU OR "MOORE JOHN TOMLIN"/AU) L3 L4

O SEA ABB=ON L1 AND L2 AND L3

279 SEA ABB=ON L1 OR L2 OR L3

3 SEA ABB=ON L5 AND ?FIBROSIS? L6 SELECT RN L6 1

FILE 'REGISTRY' ENTERED AT 10:23:47 ON 03 DEC 2009

29 SEA ABB=ON (140208-24-8/BI OR 17372-87-1/BI OR 192526-67-3/BI L7 OR 278779-30-9/BI OR 517-28-2/BI OR 635-65-4/BI OR 65666-07-1/B I OR 849654-17-7/BI OR 849654-18-8/BI OR 849654-19-9/BI OR 849654-20-2/BI OR 849654-21-3/BI OR 849654-22-4/BI OR 849654-23 -5/BI OR 849654-24-6/BI OR 849654-25-7/BI OR 849654-26-8/BI OR 849654-27-9/BI OR 849654-28-0/BI OR 849654-29-1/BI OR 849654-30 -4/BI OR 849654-31-5/BI OR 9000-86-6/BI OR 9000-97-9/BI OR 9001-60-9/BI OR 9001-78-9/BI OR 9002-02-2/BI OR 9003-98-9/BI OR 9046-27-9/BI)

FILE 'HCAPLUS' ENTERED AT 10:23:55 ON 03 DEC 2009 1 SEA ABB=ON L6 AND L7

FILE 'REGISTRY' ENTERED AT 10:25:04 ON 03 DEC 2009

STRUCTURE 278779-30-9

L10 1 SEA SSS SAM L9

L11 45 SEA SSS FUL L9

FILE 'HCAPLUS' ENTERED AT 10:28:22 ON 03 DEC 2009

4 SEA ABB=ON L11 AND LIVER FIBROSIS L12

L13 4 SEA ABB=ON L11 AND LIVER FIBROSIS+ALL

L14 10 SEA ABB=ON L11 AND (?LIVER? OR ?HEPAT?)(W)(?DISEAS? OR ?FIBROSIS?)

FILE HOME

FILE HCAPLUS

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FILE LAST UPDATED: 2 Dec 2009 (20091202/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2009

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